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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/900,754	ALLEN ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-26,28,36-39 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-26,28,36-39 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Paper filed 12 September 2005 in response to the Non-Final Office Action mailed 12 May 2005. Claims 24-26, 28-30, 32 and 36-39 were considered in the 12 May Office Action. Claims 29, 30 and 32 were canceled and claim 41 was added in the 12 September Paper. Claims 24-26, 28, 36-39 and 41 are pending and under consideration

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment and Arguments

Rejection of claims 29, 30 and 32 is rendered moot by cancellation of the claims.

Specification

The amendment filed 21 March 2005 **stands objected to** under 35 U.S.C. 132(a) because it introduces new matter into the disclosure for reasons of record and herein below.

The amendment was objected to because Applicant has amended the specification at page 10, paragraph 4, to incorporate several applications and an issued patent that had not previously been incorporated. As these disclosures were not incorporated by reference at the time of filing, their incorporation by amendment constitutes impermissible new matter added to the specification.

In response, Applicant contends that because only the disclosure of US Provisional Patent Application 60/084,194 is incorporated by reference, the amendment does not constitute new matter. Applicant's position appears to be that, because mere reference to another application, patent, or publication is not an incorporation by reference, the specification can be amended after filing to include a reference to any of these without adding new matter.

As an initial matter, it is acknowledged that application 08/971,310, which is incorporated by reference in the originally filed application, was converted to US provisional application 60/084,194. Therefore, the reference to and incorporation by reference of 60/084,194 does not constitute new matter.

With regard to the other applications and patent, it is not clear that the amended paragraph cannot be construed as constituting an incorporation by reference of all of the named applications and patents. The incorporation by reference is stated at the end of a sentence that recites all of the added serial numbers and reads, "which is incorporated herein in its entirety". It is not clear that "its" is specifically referring to the '194 provisional. In view of this uncertainty, the recitation is construed as broadly as reasonable to encompass incorporation of any or all of the named applications or patents.

Furthermore, even if one were to accept Applicant's contention that only the subject matter of the '194 application is incorporated by reference in the amended paragraph, *arguendo*, the amendment still constitutes new matter. The amended paragraph reads (emphasis denoting added text):

> In a preferred embodiment of the present invention, the tryptase targeting construct is prepared directly from a plasmid genomic library using the methods described in U.S. Patent no. 6,815,185 issued November 9, 2004, which is based on U.S. Patent Application No. 09/885,816, filed June 19, 2001, which is a continuation of U.S. Application No. 09/193,834, filed November 17,1998, now

> abandoned, which claims priority to provisional application no. 60/084,949, filed on May 11, 1998 and provisional application no. 60/184,1947, and U.S. Patent Application Ser. No.: 08/971,310, filed November 17, 1997, which was converted to provisional application no. 60/084,949, filed on May 11, 1998, the disclosure of provisional application no. 60/084194 which is incorporated herein in its entirety.

The applications and patents cited in the amended paragraph appear to be related to the original disclosure of the instant application only insofar as application 09/193,834 claims benefit of the '194 provisional. However, the '834 application also claims benefit of the '949 provisional, which would comprise information not comprised by the originally cited '310 application. In sum, there is nothing in the originally filed disclosure that would lead one to believe that the processes for preparing a tryptase targeting construct directly from a plasmid genomic library described in the variously cited patents and applications were disclosed in the originally filed application, let alone that these were the preferred embodiments for preparing a tryptase targeting construct. The statement that the newly cited applications and patent describe the preferred methods of preparing the tryptase targeting construct constitutes new mater regardless of whether the disclosures thereof are incorporated by reference because there is nothing in the originally filed disclosure to indicate that the methods described in those disclosures were contemplated as embodiments of the instant application, preferred or otherwise.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the amendment stands objected to.

Claim Rejections - 35 USC § 101/§112, first paragraph

Claims 24-26, 28 and 36-39 **stand rejected** and newly added claim 41 **is rejected** under 35 U.S.C. 101 and 112, first paragraph, because the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility for reasons of record and herein below.

Response to Arguments

In response to the *prima facie* case and arguments of record, Applicant maintains that the claims are supported by a specific and substantial credible utility.

Applicant first incorporates by reference the arguments made in the 18 March 2005 amendment (presumably the amendment entered 21 March 2005), which arguments were fully addressed in the 12 May Office Action.

Next, Applicant cites Arthur T. Sands (Industrializing Breakthrough Discovery, Current Drug Discovery, Aug. 2002, at page 21) as conclusively stating the utility of mouse knockouts. Applicant cites a passage which states, "After a decade of using mouse knockouts, the data on the predictive power in drug discovery is irrefutable" and that knock outs of drug targets are highly-predictive as to the on-target effects and side effects of drugs that act at the target. Applicant submits that in light of the arguments of record, a person of ordinary skill in the art would immediately appreciate why the invention is useful. Applicant submits that it cannot be reasonably debated that a person of ordinary skill in the art would not immediately appreciate why the invention is useful: for determining the function of the mTMT gene, for studying disease processes in which mTMT plays a role, and for drug discovery.

These arguments have been fully considered but are not deemed persuasive. Applicant is again reminded that the utility requirement 35 USC §101 requires that the disclosure provide a specific and substantial utility for the claimed invention.

With regard to using the mouse to determine the function of the mTMT gene, the previous Office Action maintains that this is not a substantial utility. As stated in previous Office Actions, with regard to "substantial utilities", MPEP 2107.01 states, "the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use and, therefore, do not define 'substantial utilities': (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved...(C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility..." There is no question that what applicant proposes to be a patentable utility is actually basic research to obtain information about the properties of the mouse itself. Applicant appears to be asserting that such a utility is substantial because the information obtained might be used, after considerable additional research to establish how what is measured in the mouse is related to the gene, to understand the properties of an mTMT gene. However, beyond contributing to the fund of scientific knowledge, which the Supreme Court in *Brenner, Comr. Pats. v. Manson* found to be insufficient to support a patentable utility (see the paragraph bridging pages 3-4 of the 12 May Office Action), the only purpose of determining the functional properties of the mTMT gene is to discover a 'real-world' utility for the mouse or the gene. This is not a patentable utility.

Likewise, Applicant's contention that the animal can be used for studying disease processes in which mTMT plays a role is not a substantial utility because there is no disclosure

of any disease processes in which mTMT plays a role. As described in previous Office Actions, neither the specification nor the art provides a specific and substantial teaching of what disease state is modeled by the animal. All of the teachings in the specification regarding the utility of the claimed animal as a disease model are general in nature and would apply to any transgenic animal exhibiting an altered phenotype. Although the specification discloses that the mouse exhibits decreased body weight, decreased thymus weight, decreased thymus weight to body weight ratio and increased pre-pulse inhibition, all relative to wild-type mice, there is no teaching what specific disease state is being modeled. The specification asserts that the transgenic animals and cells may be utilized as models for diseases, disorders, or conditions associated with phenotypes relating to a disruption in a tryptase, but provides no specific teaching as to what diseases, disorders, or conditions relate to a disruption in a tryptase. As established in the Office Action mailed 10 May 2002, the phenotype arising from disruption of any given gene in any given animal is highly unpredictable (see especially the discussion beginning in the first full paragraph on page 7). Therefore, it cannot be asserted the phenotypic characteristics disclosed for the claimed mouse are relevant to any other species of mammal comprising a disruption in an endogenous mTMT gene without additional experimentation to reasonably confirm that this is the case. Thus, the utility asserted for the claimed animal is neither specific, because the specification fails to identify the specific disease state modeled by the animal, nor substantial, because it is merely an invitation to the skilled artisan to experiment and identify which, if any, diseases are modeled by the claimed invention.

With regard to drug discovery, an assertion that the instant mouse can be used in drug discovery does not constitute a specific and substantial utility unless the skilled artisan would

know how to use the drugs discovered using the animal. As discussed herein above, neither the art nor the instant application teach how the disclosed characteristics of the claimed invention relate to pathological states such that the skilled artisan would know how to use drugs that affect those characteristics.

With regard to the teachings of Sands, it is noted that the citation appears to be from a publication of the Thompson biotechnology company, which is not a peer-reviewed journal. As such, it is not clear whether the opinions expressed therein are based on an objective analysis of the field or are meant to express a point of view that is favorable to the technologies being developed by the company. Nevertheless, although Sands does express an opinion that mice comprising knockout mutations of well-established drug targets are predictive of on-target effects and side effects of drugs that target the mutated protein, Sands does not teach that all knockout mice can be used to develop useful drugs regardless of the gene targeted. In fact, in the paragraph bridging the left and middle columns on page 21, Sands teaches, "In order to discover which genes among thousands encode breakthrough targets, industry scientists must conduct rigorous physiological assessment to determine which targets to eliminate and which to pursue." Viewed as a whole, the teachings of Sands advocate using knockout mice to search for viable drug targets and eliminate genes that might not be viable drug targets. In other words, Sands is teaching that knockout mice can be used to determine whether or not the knocked out gene would have utility for drug discovery. Again, this amounts to using the mouse to determine whether or not the gene knocked out has a real-world utility and is not substantial particularly in view of the fact that one would not know how to use a drug discovered using the mouse.

Furthermore, the Examiner has cited the teachings from articles published in independent peer-reviewed journals which demonstrate that the utility of any given knockout mouse, even as a model of gene function, cannot be assumed and must be established experimentally. For Example, on page 8 of the previous Office Action, the Examiner cites Gerlai *et al.*, who teaches:

> The functional relevance of gene targeting has been questioned because the mutation might lead to an avalanche of compensatory processes (up- or downregulation of gene products) and resulting secondary phenotypical changes. Clearly, a null-mutant organism might not only lack the product of a single gene but might also possess a number of developmental, physiological, or even behavioral processes that have been altered to compensate for the effect of the null mutation. Therefore, one might expect an array of complex phenotypical changes that might not be directly related to the function of the gene of interest. Teasing out the primary and secondary changes will require co-ordinated efforts of scientists from several fields of biology. However, these efforts might be conduced in vain if the effects of genes other than those of the one targeted have not been ruled out with certainty.

On page 17 of the previous Office Action, the Examiner cites Wolfer *et al.* who teaches that mice produced as described in the instant application will comprise not only the induced null mutation, but also 129 genes from the ES cells and a linkage disequilibrium will exist for genes linked to the target gene because animals comprising the target gene will also comprise the linked 129-derived alleles and mice that do not comprise the target gene will comprise alleles of the background strain. Thus, without experimental characterization of the animal, the skilled artisan does not know which phenotypic characteristics are a result of the target gene ablation and which are a result of linkage disequilibrium of genes linked to the target gene. On page 18, the Examiner cites Crawley *et al.* as illustrating that the phenotype exhibited by an animal comprising a homozygous ablation of a given gene is highly dependent upon genetic background by citing the example of a *HEXA* gene knockout, which in humans results in Tay-Sachs disease but produces no ill-effects in mice.

Thus, the art of record, viewed as a whole, does not support Applicant's contention that the disclosure provides a specific and substantial asserted utility or a well-established utility for claimed invention.

Applicant asserts that a claimed invention need only satisfy one of its stated objectives to satisfy the utility and enablement requirements and cites *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700 (Fed. Cir. 1999) and *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555,1571 (Fed. Cir. 1992) in arguing that an invention is useful if it is capable of providing some identifiable benefit and must be totally incapable of achieving a claimed result to lack utility.

While it is acknowledged that only a single specific and substantial credible utility need be disclosed or well-established for a claimed invention, for the reasons of record and herein, the instant invention lacks a single specific and substantial utility. With regard to the case law cited by Applicant, the statements cited therein are referring to the requirements to establish "credible" utility. The Examiner has never asserted that the utilities identified by applicant are incredible. Instead, the Examiner's position is that the utilities are either not specific to the subject matter claimed, would require additional experimentation to reasonably confirm and/or constitute use testing. That is, none of the utilities identified by Applicant are both specific and substantial.

Declaration of John Burke Pursuant to 37 C.F.R. §1.132

In response to the Examiner's noting that the phenotypic differences between the mTMT knockout mice and wild-type mice do not appear to be statistically significant, Applicant has

submitted a declaration signed by John Burke, attorney of record, showing that the phenotypic differences are statistically significant. Specifically, the declaration and supporting documentation show that the increased Prepulse Inhibition (PPI) with a 90dB prepulse (as depicted in Figure 5) is statistically significant with a 1-*p* value of 0.98 (9 wild-type mice tested and 11 mTMT knockout mice tested). Based on this, Applicant contends that additional experimentation is not required to establish the phenotypic differences are of sufficient magnitude to be useful as a model.

It is acknowledged that the data presented in the declaration (page 4 of the exhibit) demonstrate that homozygous mTMT knockout mice exhibit a significantly increased prepulse inhibition at a 90dB prepulse and 120dB pulse. However, as stated in the paragraph bridging pages 7-8 of the previous Office Action, "even if the phenotype of the claimed mouse were significantly different from a wild-type mouse, neither the specification nor the art provides a specific and substantial teaching of what disease state is modeled by the animal. With regard to pre-pulse inhibition, the specification [and declaration] teaches that the mice exhibit 'a stimulus processing phenotype opposite to that seen in schizophrenic patients' (page 53), which is not recognized as a useful model of anything. Thus, the utility asserted for the claimed animal is neither specific, because the specification fails to identify the specific disease state modeled by the animal, nor substantial, because it is merely an invitation to the skilled artisan to experiment and identify which, if any, diseases are modeled by the claimed invention." Therefore, the showings of the declaration are insufficient to overcome the rejection in view of the record as a whole.

In response to the assertion that all of the teachings in the specification regarding the utility of the claimed animal as a disease model are general in nature and would apply to any transgenic animal with an altered phenotype Applicant contends that one skilled in the art would immediately understand that mTMT knockout mice have a well-established utility as models of diseases because it was well known at the time of filing that tryptases are prominently expressed in mast cells, and that mast cells play beneficial immunosurveillance and effector roles in the body, especially during bacterial infections. Applicant asserts that the claimed mice can be used as models of disease in which mast cell function is impaired. In support of this argument, Applicant cites Caughey *et al., J Immunol.* 2000 Jun 15;164(12):6566-75 and the abstract of Malavitya *et al., J Immunol.* 1994 Feb 15; 152(4):1907-14.

Applicant further argues that it was also well known in the art at the time of filing that mast cell tryptases are implicated in allergic airway diseases, including asthma and that it was well known that tryptase inhibitors block allergic bronchoconstriction and eosinophilic inflammation in sheep. Applicant cites Caughey *et al.* as teaching that human trials of tryptase inhibitors have shown that they reduce asthmatic responses to inhaled allergen. Hence, one skilled in the art would immediately understand that the claimed mice can be used to validate mTMT as a "druggable" gene target. Applicant urges that because the claimed mice have a null allele of the mTMT gene, the claimed mice allow one to predict the likely effects-and side effects of a drug that antagonizes mTMT function. Applicant urges that inhibitors of other tryptases have been developed for the treatment of asthma in humans; therefore, the mTMT knockout mice can be used to predict the effects of a specific inhibitor of TMT in humans.

These arguments have been fully considered but are not deemed persuasive. It is first noted that, although Caughey *et al.* teaches that there is evidence that tryptases as a class of protein play a role in bronchoconstriction and eosinophilic inflammation in asthma (second paragraph on page 6566) and Malaviya teaches that mast cells play a role in host defense (although there is no mention of tryptases), Caughey *et al.* also teaches, "[t]he immunological significance of γ-tryptase [a.k.a., mTMT] expression by mast cells is not yet clear and awaits further characterization of this novel gene product's biogenesis and physical and enzymological properties" (page 6573, right column, lines 21-25). In view of this teaching, it is clear that the utility of drugs targeting the mTMT gene was not established at the time of filing. Therefore, Applicant's assertion that the mice an be used to validate mTMT as a "druggable" target amounts to assaying for or identifying a material that itself has no specific and substantial utility. That is, Applicant is asserting that the mouse can be used to assay for the properties of a drug that antagonizes mTMT; however, as neither the specification nor the art disclose a specific and substantial utility for a drug that antagonizes mTMT, using the mouse to assay the properties of the drug does not constitute a specific or substantial utility.

Applicant's assertion that the mouse can be used as model of disease in which mast cell function is impaired is also not persuasive in view of the absence of any known role of mTMT dysfunction in any disease in which mast cell function is impaired. In view of the unpredictable relationship of genotype to phenotype, the absence of knowledge as to the immunological significance of mTMT at the time of filing (Caughey *et al.*, *supra*), the absence of any evidence of impairment of mast cell function in the claimed invention, let alone any disclosed phenotype characteristic of a disease in which mast cell function is impaired, it is unclear what, if any,

disease can be modeled using the mouse. Therefore, the utility of the mouse as a model of disease in which mast cell function is impaired would have to be established experimentally.

Next, Applicant again contends that the claimed invention has a specific and substantial utility to study of the function of the mTMT gene. In support of this contention Applicant cites Doetschman as teaching that knockout phenotypes do provide accurate information concerning gene function.

This argument is not deemed persuasive. First, Applicant is again reminded that, in the absence of an established "real-world" utility for the mouse or the gene, the only purpose of determining the functional properties of the mTMT gene is to contribute to the fund of scientific knowledge or to discover a 'real-world' utility for the mouse or the gene itself, which are not patentable utilities.

Furthermore, although Doetschman states that knockout phenotypes do provide accurate information concerning gene function, this is a general statement and, in view of the art of record considered as a whole, cannot be construed as a teaching that all knockout mice are useful to study gene function and the utility of any given mouse to study gene function need not be established. In attempting to determine gene function through an analysis of behavioral or physiological testing of mice comprising a disruption of a gene, distinguishing between a phenotype that is a result of gene loss and genes of the parental strains becomes problematic. As discussed ion page 17 of the previous Office Action, in the production of the presently claimed mice, the specification states that the recombination construct is injected into a 129/sv-+P+Mgf-SLJ/J mouse ES cell which were used to produce mice on a C57BL/6 background. Wolfer *et al.*

(2002) *TRENDS Neurosci.* 25 :336-340 teaches that mice created this way will comprise not only the induced null mutation, but also 129 genes from the ES cells. Furthermore, a linkage disequilibrium will exist for genes linked to the target gene because animals comprising the target gene will also comprise the linked 129-derived alleles and mice that do not comprise the target gene will comprise alleles of the background strain. Thus, without experimental characterization of the animal, the skilled artisan does not know which phenotypic characteristics are a result of the target gene ablation and which are a result of linkage disequilibrium of genes linked to the target gene.

Furthermore, Gerlai *et al.* (1996) *Trends Neruosci.* 19:177-181, cited in the paragraph bridging pages 17-18 of the previous Office Action, teaches that the functional relevance of gene targeting has been questioned because the mutation might lead to an avalanche of compensatory processes (up- or downregulation of gene products) and resulting secondary phenotypical changes. Gerlai *et al.* teaches, "a null-mutant organism might not only lack the product of a single gene but might also possess a number of developmental, physiological, or even behavioral processes that have been altered to compensate for the effect of the null mutation. Therefore, one might expect an array of complex phenotypical changes that might not be directly related to the function of the gene of interest. Teasing out the primary and secondary changes will require co-ordinated efforts of scientists from several fields of biology. However, these efforts might be conduced in vain if the effects of genes other than those of the one targeted have not been ruled out with certainty" (page 177; emphasis added). Thus, Gerlai *et al.* clearly teaches that knowledge of a phenotype is not sufficient to enable study of gene function without additional

information as to whether the phenotype is actually related to function of the gene and how the two are related.

Still further, the general relevance a phenotype identified in a knockout mouse to gene function in other organisms must also be established experimentally. This is illustrated by Crawley (1996) *TRENDS Neurosci.* 19:181-182 (discussed in the first full paragraph on page 18 of the previous Office Action), who provides an example of a knockout of the *HEXA* gene, which in humans results in Tay-Sachs disease but produces no ill-effects in mice (see especially the paragraph bridging page 180-181). Thus, even if one could reasonably assert that the phenotypes displayed by the claimed mouse are related to the functional properties of the gene, the relevance of the phenotype exhibited by the claimed mouse to mTMT gene function in any organism other than the mouse itself must also be established experimentally.

Applicant further contends that the mice of claim 38 and claim 39 have a visible marker gene inserted into the mTMT coding sequence. Expression is therefore driven by the endogenous mTMT promoter. Applicant urges that expression of the LacZ gene indicates where the mTMT gene is expressed, and so the mice can be used to determine the expression pattern of the gene, which is a specific, substantial and credible utility.

This argument has been fully considered but is not deemed persuasive. First, it is noted that none of the claims are limited to a mouse comprising a gene encoding visible marker configured such that expression of the visible marker would provide information as to the expression of the mTMT gene. Furthermore, there is no evidence that the construct described in Figure 2 provides LacZ expression under the control of the endogenous mTMT promoter and

there is no LacZ data provided to substantiate that the mouse reduced to practice expresses LacZ. Therefore, even if one were to accept that an embodiment wherein the mouse comprises a visible marker gene such as LacZ operably linked to the endogenous mTMT promoter would meet the requirements of 35 USC §101, that embodiment does not appear to be disclosed in the instant application.

Furthermore, as there is no disclosed specific and substantial utility for the gene which applicant proposes to use the claimed invention to study, the asserted utility amounts to use testing. Similar assertions were made by the Appellants in *In re Fisher*, 04-1465, 22 (Fed. Cir. 2005). Fisher claimed that the fact that the function of the claimed ESTs was unknown was irrelevant to the utility of the invention because the ESTs can be used as research intermediates that may help scientists to isolated the particular underlying protein-encoding genes and conduct further experimentation on those genes. The overall goal of such experimentation is presumably to understand the maize genome-the functions of the underlying genes, the identity of the encoded protein, the role those proteins play during anthesis, whether polymorphisms exist, the identity of promoters that trigger protein expression, whether protein expression may be controlled, *etc.* The Court in *Fisher* found that ESTs useful to identify genes that could be used to conduct experiments to understand the function of the genes, *etc.* "are, in the words of the Supreme Court, mere 'object[s] of use-testing' to wit, objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end" (bridging pages 13-14). Likewise, a mouse useful only to study a gene having no known function is an object upon which scientific research could be performed with no assurance that anything useful will be discovered in the end.

In response to previous Arguments that the utility of a given mouse for studying the utility of a given gene is not a certainty, Applicant cites *Nelson v. Bowler and Crossley*, 206 USPQ 881 (CCPA 1980) and contends that there is no requirement in the law that there must be certainty with regard to an asserted utility. This argument is not persuasive. In the passage cited by Applicant, the Court responds to Bowler's argument that the tests are inconclusive showings of pharmacological activity since confirmation by statistically significant means, *i.e.*, a 4-point assay, occurred after the critical date by stating, "a rigorous correlation is not necessary where the test for pharmacological activity is reasonably indicative of the desired response" and "the four-point assay, while preferable, was not the sole means for establishing practical utility." In the instant case, the Application provides no evidence that the claimed invention can be used as a disease model as asserted in the specification. Therefore, in contrast to the facts in *Nelson v. Bowler* there are no disclosed test results that would indicate that the claimed invention in the instant case could be used as a disease model or that establish that the claimed invention is an accurate model of gene function.

In response to the Examiner's arguments that the relationship of the phenotype displayed by a mouse comprising a mutation in a given gene is "highly" dependent upon genetic background and therefore its utility as a model system must be established experimentally. Applicant contends that the Examiner has provided no evidence of the existence of compensatory processes with respect to the mTMT null mutation and therefore has failed to show that it is more likely than not that person skilled in the art would not consider credible any

specific and substantial utility asserted by the applicant. Applicant argues that even if such compensatory processes do indeed occur, then this establishes an additional utility for the claimed mice, namely the study of those compensatory processes.

This argument has been fully considered but is not deemed persuasive. It is again noted that the Examiner has not asserted that the utilities put forward by Applicant are not "credible". Instead, as repeatedly stated in prosecution, no single specific and substantial utility has been identified for the claimed invention. With regard to using the mouse to study compensatory responses, this is clearly an assertion that the mouse can be used to study the properties of the mouse, which properties might or might not be useful. This is not a substantial utility.

Declaration of Robert Driscoll Pursuant to 37 C.F.R. §1.132

Applicant submits a Rule 132 declaration from Robert Driscoll, Vice President of lntellectual Property & Legal Affairs of Assignee, Deltagen as evidence of sales and purpose of such use. The declaration states that the claimed mouse has been purchased by at least one pharmaceutical company. Declarant asserts that the company is one of the ten largest pharmaceutical companies in the world (although the identity of the company is not disclosed) and that the company purchased the claimed mouse for studying gene function and for human therapeutic drug development. Applicant submits that it runs contrary to common sense to think that one of the world's largest pharmaceutical corporations would purchase the claimed mouse if it thought the mouse had no utility.

The showings of the declaration are not sufficient to support Applicant's assertion of commercial success. MPEP §716.03(b) IV states, "Gross sales figures do not show commercial

success absent evidence as to market share, *Cable Electric Products, Inc. v. Genmark, Inc.*, 770 F.2d 1015, 226 USPQ 881 (Fed. Cir. 1985), or as to the time period during which the product was sold, or as to what sales would normally be expected in the market, *Ex parte Standish,* 10 USPQ2d 1454 (Bd. Pat. App. & Inter. 1988). The declaration does not include any sales figures and does not provide any evidence to establish market share, the time period during which the product was sold or evidence as to what sales would normally be expected in the market. Therefore, the declaration does not establish commercial success.

Furthermore, even if commercial success were established by the declaration, the case law cited by Applicant does not support the conclusion that a rejection under 35 USC §101 made in *Ex parte* prosecution cannot stand in the face of a purchase by a large pharmaceutical company. The passage from *Brenner v. Manson* does not suggest in any way that a single sale to a large pharmaceutical company overrides all other considerations as to the patentable utility of a claimed invention. Instead the passage speaks to the inadequacy of non-commercial utilities, such as contributions to the fund of scientific information, to establishing patentable utility.

Applicant also cites *Raytheon Company v. Roper Corporation*, 220 USPQ 592 (CA FC 1983). The passage cited therefrom reads in full

> Correct finding of infringement of otherwise valid claims mandates as matter of law finding of utility under 35 USC 101; rule is not related to fact that defendant may simultaneously assert non-utility and non-infringement; it relates to time of decision, not to time of trial, and is but common sense approach to law; if party has made, sold, or used properly claimed device, and has thus infringed, proof of that device's utility is thereby established; people rarely, if ever, appropriate useless inventions; proof of such utility is further supported when claims have on their merits been met with commercial success.

Thus, the Courts have found that commercial success supports proof of utility established by a finding of infringement. This does not support that applicant's assertion that a rejection under 35 USC §101 based on a lack of patentable utility cannot stand in view of the purchase of the claimed mouse by a pharmaceutical company. With regard to *CTS Corp. v. Piher International Corp.* 188 USPQ 419 (7th Cir. 1975), the courts finding was not that commercial success establishes utility for an invention in the absence of an asserted or well-established utility based on the properties of the invention. On page 428, the Court states, "[t]he fact that there was a defect in the prototypes surely does not demonstrate that the *invention* was not useful. Indeed, since the basic features of the invention appear to be embodied in Piher's PT-15 trimmer — as may fairly be inferred from Piher's on sale defense and CTS' original charge that the PT-15 infringes the ¢285 patent — and since Piher's trimmer is evidently a commercial success, it seems logical to infer that the subject matter of the invention is useful within the meaning of § 102." Thus, in *CTS Corp. v. Piher,* Piher had disclosed a specific and substantial utility for the claimed trimmer, the basic features of which were embodied in the disclosed trimmer. In contrast, in the instant case, no specific or substantial utility has been identified for the claimed invention.

Finally, Applicant cites a passage from *In re Fisher*, 04-1465, 22 (Fed. Cir. 2005) wherein the Court acknowledged that that commercial success may support utility of an invention. Applicant contends that, unlike Fisher, Applicant has now submitted evidence that the claimed invention has been purchased and delivered to at least one large pharmaceutical company. This argument is not deemed persuasive because, while the Court in *Fisher* acknowledges that commercial success may support utility, one would not construe this as

meaning that commercial success is all that is required to establish patentable utility. In *Fisher*, the Court does not address the requirements for overcoming a *prima facie* finding of lack of utility by establishing commercial success. In view of the record as a whole, which establishes that the utilities identified by applicant are not specific and substantial, the purchase of the claimed invention by a single pharmaceutical company for the purpose of "studying gene function and for human therapeutic drug development" does not establish that a patentable utility has been asserted in the application or would be readily apparent to the skilled artisan based on the original disclosure as required under 35 USC §101.

Applicant's arguments and the showings of the Declarations have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §101 as lacking a patentable utility and 35 USC §112, first paragraph, as lacking an enabling disclosure.

Claim Rejections - 35 USC § 112, first paragraph

Claims 24-26, 28 and 36-39 **stand rejected** and newly added claim 41 **is rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons of record and herein below.

The rejection set forth at pages 12-20 of the 12 May Office Action finds that, first, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons of record, one skilled in the art clearly would not know how to use the claimed invention. Furthermore, even if one were to accept Applicant's assertions that the disclosure satisfies the utility requirement of 35 USC §101, the skilled artisan would not

be able to use the invention as asserted by Applicant without first engaging in undue experimentation.

Although the relative level of skill in the art is high, one of ordinary skill would not be able to use the animals or cells claimed without undue experimentation. Given the unpredictable nexus of genotype and phenotype in knockout mice and the unpredictability of correlating the phenotypic characteristics of a gene knockout in a mouse with any given disease state, using the claimed invention as a disease model or to study the function of the mTMT gene as asserted would require undue experimentation. The art teaches that the phenotype exhibited by a knockout mouse might be a consequence of developmental, physiological, or even behavioral processes that have been altered to compensate for the effect of the null mutation, or might be related to the target mutation only as a consequence of disequilibrium of genes linked to the target gene. Thus, using the mouse to study the gene requires that the skilled artisan first establish that the phenotype is actually related to the functional properties of the gene and how phenotype and function are related. The art also teaches that the characteristics of an animal comprising a mutation in a target gene are highly dependent upon genetic background. Thus, the relevance of information obtained using a given knockout mouse to any organism other than the mouse itself must be carefully established before the animal can be used as a disease model. Therefore, using the mouse as asserted would require undue experimentation.

With regards to the claims to cells obtained from the mouse, the cells would not exhibit the phenotypic characteristic disclosed for the mouse and no phenotype has been disclosed for the cells. Thus, in addition to experimenting to identify a disease state modeled by the cells, the

skilled artisan would have to experiment to determine a phenotype that could be used to screen for therapeutic agents as contemplated in the specification.

Response to arguments

In response the *prima facie* case of record, Applicant cites the preceding arguments as establishing the claimed invention has a number of specific, substantial, and well- established utilities, which arguments are addressed herein above.

In response to the Examiner's statement that the specification fails to establish that the mice from which data presented in the application were generated actually comprise a mutation of the mTMT gene as recited in the claim, Applicant submits that one skilled in the art would understand based on the Figure 2 of the specification that the targeting construct has generated a null allele of the mTMT gene. Applicant asserts that targeting construct deletes bases 164 to base 287 and inserts a LacZ-neo cassette at the site of the deletion. The deletion and the insertion cause a reading frame shift that results in the appearance of stop codons in all three reading frames downstream of the insertion/deletion site. Applicant contends that one skilled in the art would immediately understand that such a profound disruption of the mTMT gene will lead to ablation of the gene's function, which is the definition of a null allele.

While Applicant's point is taken insofar as one of ordinary skill in the art would expect that the targeting vector to inactivate any gene into which it is inserted, the Examiner's point is that no genotypic analysis is presented to demonstrate that the targeting construct is actually inserted into the endogenous mTMT gene. Given that targeting vectors might be inserted at random points throughout the genome by non-homologous recombination as well as inserted into

the target gene by homologous recombination, the predicted genotype must be verified before one can reasonably state that the phenotype is in any way a result of insertion of the targeting vector into the target gene.

In response to the Examiner's statement that the phenotypic differences identified in mice are very small and do not appear to be statistically significant, Applicant refers to the Rule 1.132 Declaration of John Burke, which is discussed herein above. Based on the showings of the declaration, Applicant contends that, no further experimentation is required to establish that the phenotypic differences are of sufficient magnitude to be useful as a model.

As discussed above, it is acknowledged that the data presented in the declaration (page 4 of the exhibit) demonstrate that homozygous mTMT knockout mice exhibit a significantly increased prepulse inhibition at a 90dB prepulse and 120dB pulse. However, as stated in the paragraph bridging pages 7-8 of the previous Office Action, "even if the phenotype of the claimed mouse were significantly different from a wild-type mouse, neither the specification nor the art provides a specific and substantial teaching of what disease state is modeled by the animal. With regard to pre-pulse inhibition, the specification [and declaration] teaches that the mice exhibit 'a stimulus processing phenotype opposite to that seen in schizophrenic patients' (page 53), which is not recognized as a useful model of anything. Therefore, the showings of the declaration are insufficient to overcome the rejection in view of the record as a whole.

In response to the Examiner's contention that the specification fails to teach what disease state is modeled by the claimed invention, Applicant contends that one skilled in the art would be aware of a number of disease states that were known in the art at the time of filing in which mTMT was implicated e.g. asthma. In addition, Applicant asserts that there are numerous other

uses of the claimed mouse, referred to above, that would be immediately understood by those skilled in the art such as to study expression of mTMT using LacZ staining and to study the function of the mTMT gene by, for example, studying the phenotypes resulting from mTMT disruption.

Applicant dismisses the teachings of Gerlai, which indicate that the relationship of the phenotype to genotype must be established experimentally before useful information about the function of the target gene can be obtained. Applicant contends that Gerlai indicates that such "compensatory processes" might occur based on a small number of examples involving unrelated genes. Applicant contends that Gerlai does not stand for the general proposition that knowledge of a phenotype is always insufficient to study gene function.

Likewise, Applicant dismisses the teachings of Crawley *et al.*, which demonstrate that the phenotype exhibited by an animal comprising a homozygous ablation of a given gene is highly dependent on genetic background and, therefore, the relevance of any given knockout animal to any other animal is unpredictable. Applicant contends that Examiner is relying on art which shows what might be the case with respect to the mTMT gene based on results obtained for other completely unrelated genes and urges that such speculative arguments demonstrate that the Examiner has failed to show the requisite degree of unpredictability.

Likewise, Applicant dismisses the teachings of Wolfer *et al.*, which teaches that an additional source of unpredictability in establishing the relationship of the phenotype displayed by a knockout mouse to the properties of the target gene is the possibility of a disequilibrium of genes linked to the target gene. Applicant notes that, according to Wolfer et al., "...the possibility exists that an apparent effect of a null mutation could be due to a flanking 129 gene.

Generally, the problem is disregarded because it imposes control strategies deemed costly, and because the statistically expected number of confounding flanking genes is relatively low". Applicant contends that a phenotype caused by liked genes is a rare phenomenon and, therefore, the phenotypic characteristics of the claimed mouse are predicable and highly likely to result from ablation of the target gene.

Applicant contends that the Examiner's arguments would seem to suggest that such unpredictability-caused either by linkage disequilibrium, or background, or "compensatory processes"-would lead one skilled in art to regard the creation of knockout mice a futile endeavor. Applicant urges that this is clearly not the case and contends that there are literally thousands of knockout mice currently being used around the world to develop drugs, validate gene targets for drugs, and to study gene function. Applicant urges that those skilled in the art do not regard the issues of linkage disequilibrium, background, and "compensatory processes" as insurmountable obstacles to using knockout mice. Moreover, Applicant asserts even if these issues must be routinely addressed for every single knocked-out gene-as the Examiner contends-then such routine investigation could not, by definition, constitute undue experimentation.

These arguments have been fully considered but are not deemed persuasive. It should be made clear that the relevant question is not whether knockout mouse, as a class of invention, are useful. The Examiner has never asserted, "the creation of knockout mice is a futile endeavor". Instead, the Examiner's position is that the utility of any given knockout mouse must be established experimentally because the relationship of phenotype and genotype in a knockout mouse is unpredictable, as is the relevance of the phenotype exhibited by a knockout mouse to disease processes in any other species of mammal.

With regard to modeling asthma, as Applicant newly asserts, there is nothing of record that would reasonably establish the claimed invention as a model of asthma. This assertion appears to be based on the teachings of Caughey *et al.*, who teaches that there is evidence that tryptases as a class of protein play a role in bronchoconstriction and eosinophilic inflammation in asthma (second paragraph on page 6566). However, as discussed herein above, Caughey *et al.* also teaches, "[t]he immunological significance of γ-tryptase [mTMT] expression by mast cells is not yet clear and awaits further characterization of this novel gene product's biogenesis and physical and enzymological properties" (page 6573, right column, lines 21-25). Thus, establishing that the claimed invention can be used as a model of asthma would clearly require undue experimentation.

Likewise, developing the claimed invention such that it can be used be used to study the function of the mTMT gene by, for example, studying expression patterns or phenotypes resulting from mTMT disruption would also require undue experimentation. As an initial matter, it is noted that none of the claims are limited to a mouse comprising a gene encoding visible marker configured such that expression of the visible marker would provide information as to the expression of the mTMT gene. Furthermore, there is no evidence that the construct described in Figure 2 provides LacZ expression under the control of the endogenous mTMT promoter and there is no LacZ data provided to substantiate that the mouse reduced to practice expresses LacZ. Therefore, even if one were to accept that an embodiment wherein the mouse comprises a visible marker gene such as LacZ operably linked to the endogenous mTMT promoter would be enabled, that embodiment does not appear to be disclosed in the instant application.

Furthermore, the teachings of Gerlai, Crawley *et al.* and Wolfer *et al.* demonstrate that one cannot assume that a knockout mouse is useful as a disease model or model of gene function. As stated herein above, the art teaches that the phenotype exhibited by a knockout mouse might be a consequence of developmental, physiological, or even behavioral processes that have been altered to compensate for the effect of the null mutation, or might be related to the target mutation only as a consequence of disequilibrium of genes linked to the target gene. Thus, using the mouse to study the gene requires that the skilled artisan first establish that the phenotype is actually related to the functional properties of the gene and how phenotype and function are related. The art also teaches that the characteristics of an animal comprising a mutation in a target gene are highly dependent upon genetic background. Thus, the relevance of information obtained using a given knockout mouse to any organism other than the mouse itself must be carefully established before the animal can be used as a disease model or a model of gene function.

Applicant's contention that the evidence presented in the art does not stand for the general proposition that knowledge of a phenotype is always insufficient to study gene function or that results obtained for other completely unrelated genes are speculative is not persuasive because the art is cited to evidence the unpredictable nature of the art. The point is precisely that the skilled artisan does not know whether the claimed invention is useful or, if it is, how it can be used.

With regard to Applicant's assertion that Wolfer *et al.* teaches that a phenotype caused by linked genes is a rare phenomenon, this is a mischaracterization of the reference. As acknowledged by Applicant, Wolfer *et al.* teaches that the possibility that an apparent effect of a

null mutation could be due to a linked gene is disregarded because it imposes control strategies that are costly. Wolfer *et al.* also states, "the statistically expected number of flanking genes is relatively low". Wolfer *et al.* does not teach that a phenotype caused by linked genes is a "rare phenomenon". In contrast, Wolfer *et al.* is clearly concerned with problems arising from flanking genes (see especially the discussion bridging pages 337-338) and recommends strategies to overcome the problem (see especially the discussion on pages 338-339; it is noted that the breeding strategies taught by Wolfer *et al.* were not available until after the instant application was filed).

Applicant's contention that the fact that experimentation may be complex does not necessarily make it undue is acknowledged. With regard to the legal standard for "undue experimentation", *In re Wands* is clear, "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* ...They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims" (8 USPQ2d 1400, page 1404). Applicant's contention that the amount of experimentation required to develop the claimed mouse such that it could be used appears to be Applicant's opinion of what is routine experimentation and not the legal analysis set forth in *In re Wands*. In contrast, analysis of the instant claims according to the "Forman factors" is clearly set forth in the 12 May Office Action, and the arguments and evidence provided by Applicant to rebut the *prima facie* case have been found unpersuasive for the reasons set forth herein above.

Applicant's arguments and the showings of the Declaration have been fully considered but are not deemed persuasive in view of the record as a whole. For these reasons, the skilled artisan would not be able to use the claimed invention as asserted by applicant without first engaging in undue experimentation to further develop what is claimed. Therefore, the claims are properly rejected under 35 USC §112, first paragraph.

Claim Rejections - 35 USC § 112, second paragraph

Rejection of claims 24, 28-30, 32 and 36-39 under 35 U.S.C. 112, second paragraph, as being indefinite is **withdrawn**. Applicant argues persuasively that "wild-type control" is a term of art which would not be unclear to one of ordinary skill in the relevant art.

New Grounds for Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

First, the claim is directed to "the transgenic mouse of claim 1". As claim 1 has been canceled, it is clear that claim 41 cannot depend therefrom. The meets and bounds of the claim are indefinite because it is not clear from which claim Applicant intends that claim 41 depend. Therefore, it is unclear what limitations are comprised by the claim. In the interest of compact

prosecution, the claim has been construed according to its broadest reasonable scope as depending from claim 24 and amending the claim accordingly would be remedial.

Claim 41 is further indefinite in reciting that the gene encodes mRNA which comprises sequence "corresponding to the cDNA sequence of SEQ ID NO: 1" and reciting that the exogenous DNA replaces the nucleotides in the endogenous mTMT gene which "correspond to nucleotides 164 to 287 of SEQ ID NO: 1". As there are various ways that a nucleic acid sequence might "correspond" to another sequence it is unclear what is encompassed by a sequence corresponding to the cDNA sequence of SEQ ID NO: 1. For example, must the corresponding sequence comprise the reference sequence, must it share some degree of homology with the reference sequence, must it be complementary to the corresponding sequence? Given that there is no definition of how correspondence to a reference sequence is determined, the metes and bounds of the claim are unclear.

It would appear that Applicant's intention is that claim 41 capture the limitations illustrated in Figure 2, which depicts the targeting vector used to establish the mTMT knockout mouse (specification page 48, lines 8-14). If this is the case, it is suggested that the claim read as follows:

"The transgenic mouse of claim 24, wherein said exogenous DNA comprises a LacZ-Neo cassette and replaces the nucleotide sequence set forth as nucleotides 164-287 of SEQ ID NO: 1."

The specification at page 7, lines 1-5, defines "tryptase gene" as a sequence comprising SEQ ID NO: 1 or comprising the sequence encoding the tryptase gene identified in GeneBank as Accession No. AF175523; GI: 6103630, both of which comprise nucleotides 164 to 287 of SEQ

ID NO: 1. Therefore, an endogenous mouse transmembrane tryptase gene as defined in the specification comprises the sequence of nucleotides 164-287 of SEQ ID NO: 1 and a transgenic mouse whose genome comprises the targeting vector of Figure 2 inserted into the endogenous transmembrane tryptase gene would comprise a LacZ-Neo cassette replacing the nucleotide sequence set forth as nucleotides 164-287 of SEQ ID NO: 1.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636